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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/114,973	07/14/98	DOVE W	960296.95491

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1633	6

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/114,973	Dove et al.
Examiner	**Group Art Unit**
Kris Pelham Mayo	1633

☒ Responsive to communication(s) filed on *Sep 21, 1999* .

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-25* is/are pending in the application.

Of the above, claim(s) *7-10* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-6 and 11-25* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☒ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *2*

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Election/Restriction

Claims 1-25 are pending in the instant application. Examiner acknowledges Applicant's Response to Requirement for Restriction, filed as Paper Number 5. Examiner acknowledges, as suggested by Applicant, that the genetically altered mouse of Group IV is indistinct from the method to identify segregating mutations of Group I, as the mouse could not be made independent of said method. Applicant's arguments to combine Groups II and III with Group I, however, are not persuasive. Groups II and III are drawn to different methods. In U.S. restriction practice, it is considered proper to restrict different methods if they have different modes of operation, different functions, or different effects. (MPEP 806.04, MPEP 808.01) Group II is drawn to a method of identifying mutations following treatment with mutagens, and Group III is drawn to a method of identifying a human genetic sequence corresponding to a segregating mutation. The inventions are unrelated because they are drawn to non-equivalent, patentably distinct methods and would involve different process steps, technical strategies and functions, and would require both a divergent search and different considerations. Because Groups I and IV are related as a genetically altered non-human animal/mouse and method of making said genetically altered non-human animal/mouse, the groups will be recombined, and prosecuted together. Therefore, claims 1-6, and 11-25 are under examination. Claims 7-10 are withdrawn from further consideration, as being drawn to a non-elected invention.

Information Disclosure Statement

The information disclosure statement filed on 23 October 1998 as Paper Number 2, does not fully comply with the requirements of 37 CFR 1.98 because: a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed is required. There is no copy of the "Cancer Economics" Supplement to the Cancer Letter, September 1996, in the file, and the information referred to therein has not been considered. Please see attached copy of the Information Disclosure Statement.

Drawings

Formal drawings were submitted by Applicant and have been approved by the PTO draftsperson.

Specification

The disclosure is objected to because of the following informalities:

Several minor typographical errors exist such as those found on page 13, line 16 - "screened".

Appropriate correction of all typographical errors is necessary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3, 5, 6, 11, and 25 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 and 9 of U.S. Patent No. 5,780,236. Although the conflicting claims are not identical, they are not patentably distinct from each other because:

1. Whereas the scope of claims 1, 3, 5, 6, 11, and 25 of the instant application includes all non-human animals and genetic loci, the scope of claims 1-6 and 9 of US 5,780,236 ('236) is limited to mice and murine genetic loci. The scope of the instant application is similarly limited to mice and murine genetic loci. See Claim Rejections, *infra*.

2. Whereas the scope of claims 1, 3, and 5 of the instant application is not limited to an isogenic index inbred strain, the dependent claim 6 of the instant application does further limit the claims to an isogenic index inbred strain. The scope of the instant application, in this regard, is equal to the scope of claims 1-6 and 9 of '236.

3. Claims 1, 3, 5, and 6 limit the index inbred strain to being genetically distinguishable from the founder inbred strain. This limitation is not specifically claimed in '236. However, the limitation is inherent to the characteristics of the index inbred strain, as claimed in '236, for the purpose of identifying a segregating mutation at a genetic locus. Identification of the segregating mutation at a genetic locus would not be possible if the index inbred strain was not genetically distinguishable from the founder inbred strain.

4. Claims 1, 3, 5, 6 and 11 identify various generations by different labels than claims 1-6 and 9 of '236. However, since the crosses are the same and the label given to each generation is arbitrary, the claims are considered as being patentably indistinct in this regard.

5. Whereas claims 1, 3, 5, and 6 recite the limitation "at least some of the N2 backcross progeny...", claim 1 of '236 recites the limitation "half of". Although the scope of the claims in the instant application is broader than that of '236, the differences are not considered to be patentably distinct in this specific case.

6. Claim 3 of the instant application recites the limitation "extreme outlying phenotype"; this limitation is encompassed by the scope of claims 1-6 and 9 of '236 which recite "outlying phenotype".

7. Claim 6 of the instant application recites the limitation "...that carries single nucleotide polymorphisms". No limitation in this regard is made in claims 1-6 and 9 of '236, therefore, claim 6 of the instant application is encompassed by claims 1-6 and 9 of '236.

8. Whereas claim 11 of the instant application recites "...the founder inbred strain carrying random point mutations...", claim 1 of '236 recites the limitation, "...the founder isogenic inbred strain being heterozygous only for random point mutations...". Heterozygosity for the random point mutations is inherent to the invention of the instant application because, as taught on page 2 of the specification, homozygotes for the mutation die in utero (see lines 23-24). Therefore, claim 11 of the instant application is not patentably distinct from claim 1 of '236 in this regard.

9. Claim 11 of the instant application recites the limitation, ".....also exhibit a modified index phenotype", whereas claim 1 of '236 does not recite any limitation to this regard. It is inherent, however, that Gen1 progeny that carry the dominant allele will also exhibit a modified index phenotype. Therefore, the invention of claim 11 of the instant application is encompassed within the scope of claim 1 of '236 in this regard.

The subject matter of claims 1, 3, 5, 6, 11, and 25 of the instant application, therefore, is encompassed by the embodiments of the claims in '236 and allowance of claims 1, 3, 5, 6, 11, and 25 of the instant application would unfairly extend the length of the patent rights to U.S. 5,780,236.

Claims 17-24 are also rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 and 9 of U.S. Patent No. 5,780,236. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 17-24 of the instant application are drawn to the non-human animal/mouse made by the methods of the preceding claims. The genetically altered mouse of claims 17 and 18 in the

instant application is made by the method of claim 11 and its dependent claims of the instant application. As elucidated above, claim 11 of the instant application is patentably indistinct from claims 1-6 and 9 of '236. The non-human animal/mouse of claims 19 and 20 in the instant application is made by the method of claim 1 and its dependent claims of the instant application. As elucidated above, claim 1 of the instant application is patentably indistinct from claims 1-6 and 9 of '236. The non-human animal/mouse of claims 21 and 22 in the instant application is made by the method of claim 11 and its dependent claims of the instant application. As elucidated above, claim 11 of the instant application is patentably indistinct from claims 1-6 and 9 of '236. Finally, the non-human animal/mouse of claims 23 and 24 of the instant application is made by the method of claim 1 and its dependent claims of '236. As Applicant pointed out in their Response to Requirement for Restriction, the mouse cannot be made independent of the methods claimed. Therefore, the mouse is obvious over the identification of the segregating mutation and methods of crossing as claimed in '236.

The subject matter of claims 17-24 of the instant application, therefore, is fully encompassed by the embodiments of the claims in '236 and allowance of claims 17-24 of the instant application would unfairly extend the length of the patent rights to U.S. 5,780,236.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any

> person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 11-16, 19-23, and 25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a mouse and a murine genetic locus, does not reasonably provide enablement for any and all non-human animals, and any and all genetic loci. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are drawn to any and all non-human animals, as in claims 19- 23. However, the specification is only enabling for the mouse. It is not known whether the specifically enabled allele and locus exists in all other non-human animals, nor is it known what effect, if any, the mutagen would have on the genotype and phenotype of those animals. Furthermore, it is not known whether the mutation would be preserved through the enabled breeding regimen of the claimed invention, such that the method for identifying a segregating mutation would be enabled.

The claims are further drawn to any and all genetic loci, as in claims 1-6, 11-16, and 25. However, as explained *supra*, the specification is only enabling for the murine genetic locus.

Claims 1-6, 11-16, 19-23, and 25 are extremely broad, encompassing any and all non-human animals, and any and all genetic loci. The courts have stated that reasonable correlation must exist between scope of exclusive right to patent application and scope of enablement set forth in patent application. See 27 USPQ2d 1662 *Ex parte Maizel*. Scope of Enablement is

considered in view of the Wands factors (MPEP 2164.01 (a)). In view of the quantity of experimentation necessary to determine the parameters listed above, the lack of direction or guidance provided by the specification, the absence of working examples for the demonstration or correlation to any and all non-human animals and any and all genetic loci, the unpredictable state of the art with respect to genotypic and phenotypic outcomes of all the various possible crossing combinations, and the breadth of the claims to any and all non-human animals, and any and all genetic loci, it would have required undue experimentation for one skilled in the art to make and/or use the invention as broadly claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6, and 11-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are indefinite in their recitation of "at least some of" and "some of", as in claims 1-6, and 11-25. It is not clear how many this phrase refers to. In the absence of specific guidance in the specification, the metes and bounds of the claimed invention cannot be determined. It is recommended that the specific number of progeny be incorporated into the claim language.

The claims are further indefinite in their recitation of "extreme", as in claims 3 and 4. It is not clear as to what defines an "extreme outlying phenotype". The definition given by Applicant on page 13 of the specification is still indefinite, and in the absence of guidance, the metes and bounds of the claimed invention cannot be determined. It is recommended that the specific phenotype be incorporated into the claim language.

The claims are further indefinite in their recitation of "enhancing effect", as in claim 14. It is not clear what specific effect this refers to. In the absence of guidance in the specification, the metes and bounds of the claimed invention cannot be determined. It is recommended that the specific phenotypic effect be incorporated into the claim language.

The claims are further indefinite in their recitation of "suppressed phenotype", as in claim 14. It is not clear what specific suppression this refers to. In the absence of guidance in the specification, the metes and bounds of the claimed invention cannot be determined. It is recommended that the specific phenotypic suppression be incorporated into the claim language.

The claims are further indefinite in their recitation of "the mouse", as in claims 17 and 18. It is not clear which mouse this phrase refers to, the genetically altered mouse or the first inbred mouse strain. In the absence of guidance in the specification, the metes and bounds of the claimed invention cannot be determined. It is recommended that the specific mouse be incorporated into the claim language.

The claims are further indefinite in their recitation of "a mouse", as in claim 18. It is not clear which mouse this refers to, since multiple mice are referenced in the independent claim 17.

In the absence of guidance in the specification, the metes and bounds of the claimed invention cannot be determined. It is recommended that the term "the mouse" be incorporated into the claim language, meaning the genetically altered mouse of claim 17.

The claims are further indefinite in their recitation of "where", as in claims 23-25. The recitation of "where" as a transitional word is confusing and indefinite with regard to its antecedent. It is recommended that the term "wherein" be incorporated into the claim language.

The claims recite the limitation "the characteristic genetic background", as in claims 17 and 18. There is insufficient antecedent basis for this limitation in the claim. No prior reference is made of a characteristic genetic background, and in the absence of such, it is unclear what this refers to. In the absence of clarity, the metes and bounds of the claimed invention cannot be determined.

The claims recite the limitation "the outlying phenotype", as in claims 19, 20, and 23-25. There is insufficient antecedent basis for this limitation in the claim. No prior reference is made to an outlying phenotype, and in the absence of such, it is unclear what this refers to. Furthermore, it is not clear what is meant by an outlying phenotype. The specification seems to teach the first or last tenth percentile of the age at death distribution, but in the absence of clarity, the metes and bounds of the claimed invention cannot be determined.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-6, and 11-25 are rejected under 35 U.S.C. 102(a) as being anticipated by Bilger et al. (1996). See entire article, especially page 251, column 2 - page 253, column 2. Bilger et al. teaches a method for identifying the Min allele at the murine Apc locus that modifies the phenotype of multiple intestinal neoplasia in B6-Min mice. The methods and mice taught by Bilger et al. comprises the steps of outcrossing a BTBR mouse to a B6-Min mouse, the B6-Min mouse carrying the Min allele at the murine Apc locus, which confers the phenotype of multiple intestinal neoplasia. Bilger et al. also teach backcrossing the B6-Min x BTBR mice to verify that the outlying phenotype is caused by a segregating mutation. The authors also teach that BTBR mice carry a phenotype-modifying tumor susceptibility allele that confers greater susceptibility than any of the other crosses carried out by the authors, which could be considered an extreme outlying phenotype. The index inbred strain of Bilger et al. is an isogenic index strain that carries single nucleotide polymorphisms (the B6-Min mouse). The authors also disclose mouse crosses

wherein the genetic background has a modifying effect on the index phenotype (reduces susceptibility to multiple intestinal neoplasia), and does not have a modifying effect on the index phenotype (does not reduce susceptibility to multiple intestinal neoplasia). Furthermore, the authors disclose mapping the location of the modifying allele (Mom1), through multiple generations of backcrossing, and evaluating the progeny of the mapping cross. The methods of Bilger et al., therefore, therefore, meet the limitations of the claimed invention of the instant application, as claimed in claims 1, 3-6, and 11-25.

Claims 1, 3, and 11, 17, and 19-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Shedlovsky et al. (1986). Shedlovsky et al. disclose a method for identifying a segregating mutation (l) at a murine genetic locus which causes an outlying phenotype (prenatal lethal) relative to an index phenotype (T/t) comprising steps of (a) outcrossing an inbred mouse strain (BTBR), mutagenized with ENU which produces random point mutations, with the index inbred mouse strain (T/t) to produce Gen1, the founder strain, heterozygous for point mutations; (b) crossing the founder mice with Bt strain; (c) backcrossing progeny to the founder parent; (d) verifying that a subset of the Gen2F_1 offspring carries the outlying phenotype; and (e) the mice made by said method (see page 135, last paragraph bridging page 136 and page 136 at "3. Results"). The methods and mice of Shedlovsky et al., therefore, meet the limitations of the claimed invention of the instant application, as claimed in claims 1, 3, 11, 17, and 19-25.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2, 5, and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shedlovsky at al., further in view of Moser et al (1990) and Dietrich et al. (1993). Claim 2 is drawn to a method of employing preserved gametes in the crosses, and claims 5 and 18 are drawn to the dominant Min allele at the Apc locus. As elucidated, *supra*, Shedlovsky et al. teach the crosses of the claimed invention. Shedlovsky et al., however, do not teach the use of preserved gametes in the crosses or the Min allele at the Apc locus. However, Moser et al. teach mouse germline mutagenesis to permit the identification of mutant genes which occur infrequently in nature. See page 324, column 1. Furthermore, Dietrich et al. teach the Min allele at the Apc locus. See page 631, penultimate paragraph. Therefore, it would have been *prima facie* obvious at the time the invention was made, for one of ordinary skill in the art to combine the above references and combine the crosses, as taught by Shedlovsky et al. with the use of preserved gametes from mouse germline mutations, as taught by Moser et al., and the Min allele at the Apc locus, as taught by Dietrich et al. to arrive at the method of employing preserved gametes in the crosses, wherein the dominant allele claimed in the crosses is the Min allele at the Apc locus, of the claimed invention. Furthermore, one of ordinary skill in the art would have had a reasonable

expectation of success, and employed preserved gametes for the benefit of performing and enhanced modification of reducing cost and increasing convenience in performing said crosses.

Conclusion

No claim is allowed, for the reasons outlined above.

The above rejections are agreed to by the Group Director.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kris Pelham Mayo whose telephone number is (703) 306-5877. The examiner can normally be reached on Monday-Friday from 8:00 a.m. to 4:30 p.m. (Eastern Time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jasemine Chambers, can be reached at (703)308-2035. The FAX phone number for group 1600 is (703)308-4242.

An inquiry of a general nature or relating to the status of the application should be directed to the group receptionist whose telephone number is (703)308-0196.

Kris Pelham Mayo, D.V.M.
Patent Examiner
Art Unit 1633
December 6, 1999

Deborah Clark
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APPROVED
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